OS-10002

1: TEK TEK tyrosine kinase, endothelial [*Homo sapiens*]

GeneID: 7010 updated 25-Jan-2009

Summary

Official Symbol	TEK (provided by HGNC)
Official Full Name	TEK tyrosine kinase, endothelial (provided by HGNC)
Primary source	HGNC:11724
See related	Ensembl:ENSG00000120156; HPRD:02571; MIM:600221
Gene type	protein coding
RefSeq status	REVIEWED
Organism	*Homo sapiens*
Lineage	*Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo*
Also known as	TIE2; VMCM; TIE-2; VMCM1; CD202B; TEK
Summary	The TEK receptor tyrosine kinase is expressed almost exclusively in endothelial cells in mice, rats, and humans. This receptor possesses a unique extracellular domain containing 2 immunoglobulin-like loops separated by 3 epidermal growth factor-like repeats that are connected to 3 fibronectin type III-like repeats. The ligand for the receptor is angiopoietin-1. Defects in TEK are associated with inherited venous malformations; the TEK signaling pathway appears to be critical for endothelial cell-smooth muscle cell communication in venous morphogenesis. TEK is closely related to the TIE receptor tyrosine kinase. [provided by RefSeq]

Genomic regions, transcripts, and products

Go to reference sequence details

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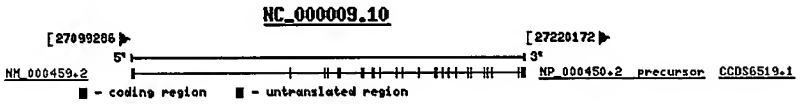

Genomic context

chromosome: 9; **Location:** 9p21

See TEK in MapViewer

Bibliography

Related Articles in PubMed

PubMed links

GeneRIFs: Gene References Into Function

1. These data show that a sporadic disease may be explained by somatic changes in a gene causing rare, inherited forms and pinpoint TIE2 pathways as potential therapeutic targets for venous malformations.
2. Observational study of gene-disease association. (HuGE Navigator)

3. Patients with preeclampsia and those with small-for-gestational-age fetuses have lower plasma soluble Tie 2 than women with normal pregnancies.
4. the strongest immunoreactivity for Tie-2 observed in cytotrophoblasts, ACC and endothelial cells of the very early human placenta.
5. Although STAT1 phosphorylation required JNK and p38MAPK activation, only JNK activation was essential for IRF1 promoter activation by Tie2-R849W.
6. Data show that Angiopoietin 1 bridges Tie2 at cell-cell contacts, resulting in trans-association of Tie2 in the presence of cell-cell contacts, while in isolated cells extracellular matrix-bound Ang1 locates Tie2 at cell-substratum contacts.
7. Data show that Angiopoietin 1 induces unique Tie2 complexes in mobile and confluent endothelial cells.
8. Observational study and clinical trial of gene-disease association, gene-environment interaction, and pharmacogenomic / toxicogenomic. (HuGE Navigator)
9. First report on role of angiopoietin 2/Tie2 in regulation of HIF-1 alpha/vascular endothelial growth factor (VEGF) expression provides additional evidence of intrinsic coordination that occurs among these factors during angiogenesis.
10. Results describe the expression of angiopoietin-1, 2 and 4 and Tie-1 and 2 in gastrointestinal stromal tumors, leiomyomas and schwannomas.
11. Data show that angiopoietin 1 induces Tie1 phosphorylation in endothelial cells, and that this phosphorylation is Tie2 dependent.
12. VEGF regulates angiopoietin-Tie2 signaling by inducing proteolytic cleavage and shedding of Tie2 via a novel PI3K/Akt-dependent pathway.
13. Activation of Tie1 ectodomain cleavage increases cartilage oligomeric protein angiopoietin 1 activation of Tie2.
14. Ang-1 phosphorylates Tie-2 and its downstream effector phosphatidylinositol 3-kinase. This induces activation of one endogenous GTPase, Rac1, and inhibition of another, RhoA
15. Tie-2(+) AMLs in endothelial culture medium supplemented with VEGF and angiopoietins resulted in their partial endothelial differentiation.
16. TIE2 expression in human blood monocytes (TEMs)identifies a distinct subset of monocytes that represent the main monocyte population in the blood and tumors of cancer patients. Purified TEMs, but not TEM-depleted monocytes, markedly promoted angiogenesis.
17. Tie2 signaling is an important angiogenic mediator that links the proinflammatory cytokine TNF alpha to pathologic angiogenesis.
18. an important role for a PECAM1-SHP2-Tie2 pathway in flow-mediated signal transduction.
19. Tie2 mediates internal translation initiation
20. In advanced arteriosclerotic lesions, the activation of the Tie2-mediated STAT5 signaling pathway may negatively regulate vessel growth.
21. The Ang-Tie2 system appears to have an autoregulatory feedback system that may be regulating the overall activity of the Tie2 system in both physiological and pathological conditions.
22. results indicate that there is a difference in the Ang/Tie2 gene expression between physiological and pathological angiogenesis in the ovary.
23. Tie2 up-regulation is associated with infiltrating breast carcinoma
24. Role of Tie2 in the differentiation of endothelial cells during angiogenesis.
25. Tie-2/Tek expression proved more sensitive than CD31 expression in terms of prognostic significance
26. the isolated receptor-binding domain of Ang1 is capable of mediating some effects of full-length Ang1 independently of Tie2 phosphorylation, possibly through integrin ligation
27. Participation of down-regulated TIE-2 in the placental tissues may indicate a role for this angiogenic factor in the development of placenta accreta.
28. the relationship of angiopoietin-1, angiopoietin-2 and tie-2 to coronary collateral formation in patients with coronary artery disease
29. Shear stress activates Tie2 receptor tyrosine kinase in vascular endothelial cells.
30. Tie-2-expressing monocytes (but not lymphocytes or granulocytes) present in human peripheral blood respond to angiopoietin-2 with both chemotaxis and altered cytokine release.

31. Angiopoetin-Tie2 autocrine pathway works in primary acute meylocytic leukemia cells or not by using soluble Tie2-Fc, which inhibits Angiopoietins from binding to Tie2 receptor.
32. Dominant Ang-2 expression against Ang-1 through Tie2 receptor in the presence of VEGF plays a critical role in initiating early neovascularization and transformation of noncancerous liver to hepatocellular carcinoma.
33. Endothelial Tie2 interacts with ABIN-2.
34. Blocking Akt function abolishes angiopoietin 1 (Ang1), a ligand for Tie2, mediated EC survival, and activating Akt rescues a Tie2 blockade-induced EC apoptosis.
35. Tie2 mRNA and protein were up-regulated in the pathogenesis of hemangioma.
36. a mutation of glycine to aspartic acid at the second glycine of the GXGXXG motif of Tie2 (G833DTie2) in human intramuscular haemangiomas (IMHs) of the capillary type
37. proper oligomerization of Ang1 having at least four subunits by the intermolecular disulfide linkage involving cysteines 41 and 54 is critical for Tie2 binding and activation
38. Vascular endothelial growth factor modulates the Tie-2:Tie-1 receptor complex
39. Stable interaction between integrin alpha5beta1 and Tie2 receptor regulates endothelial cell response to Ang-1.
40. the uORFs within the Tie2 5' UTR serve to decrease the percent of ribosomes competent for reinitiation as these traverse the mRNA 5' UTR, thus minimizing interference with the internal ribosome entry site
41. there is a novel interaction between Tie2 with the adapter molecule ShcA that may play a role in the regulation of migration and three-dimensional organization of endothelial cells induced by angiopoietin-1
42. Tie-2 signaling synergistically amplifies and participates in TNF-alpha-mediated angiogenesis.
43. findings demonstrate that in response to angiopoietin-1, Tie2 is rapidly internalized & targeted for degradation; angiopoietin-2 only weakly activated Tie2 & did not significantly stimulate receptor internalization, while mildly inducing Tie2 degradation
44. expression of NERF2 was increased under hypoxia and that this increase temporally correlated with the increase in Tie2 expression. Hypoxia-induced expression of NERF2 and Tie2 was blocked by angiopoietin-2 a competitive inhibitor of angiopoietin-1
45. presence of Tie-2 in human peripheral and autonomic nervous tissue, suggesting a role for Tie-2 in neural tissue.
46. angiopoietin 1 stimulates directed migration and possibly inhibits vascular endothelial growth factor-induced eosinophil chemotaxis via its Tie-2 receptor.
47. In a series of immunohistochemical analysis on human ovarian tissues, there was a unique localization of Tie-2 to the primary cilia of ovarian surface epithelium.
48. 2.4 A crystal structure of the Angiopoietin-2 (Ang2) receptor binding region was determined.
49. Ang1 has a role in lymphatic vessel endothelial proliferation, Tie2 expression, and VEGFR-3 upregulation
50. activation of tie-2 receptors by Ang-1 triggers the production of ROS through activation of NADPH oxidase
51. Screening for Wnt5a-regulated genes in cultured endothelial cells identified several encoding angiogenic regulators, including matrix metalloproteinase-1, an interstitial collagenase, and Tie-2, a receptor for angiopoietins.
52. Foxo-1 and Ang-2/Tie2 are part of the molecular response to shear stress, which may regulate angiogenesis.
53. comparison of the hematopoietic and angiogenic abilities of human cord blood CD34+TEK+ and CD34+TEK- cells using a clonogenic assay and xenotransplantation into immunodeficient NOD/SCID mice showing TEK plays a crucial role
54. Results showed that Tie-2 mRNA and protein expression from the eutopic endometrium did not differ significantly between endometriosis patients and normal controls.
55. sAng-2 and sTie-2 play a role in progression of some haematological malignancies
56. tyrosine residue 1106 on Tie2 is critical for coupling downstream cell migration signal transduction pathways with Angiopoietin 1 stimulation in endothelial cells
57. Tie-2 receptor is expressed by human neutrophils whose active site ligation with either angiopoietin-1 or angiopoietin-2 exerts migratory effects on the one hand and arrests VEGF-mediated chemotaxis on the other

58. expression and function of TIE2 in hematopoietic stem cells in cord blood
59. Angiopoietin-1 is implicated in the maturation and remodeling of the vascular network during embryo development and in adult life through its tyrosine kinase receptor Tie-2 stimulates endothelial cells to migrate and change shape.
60. The autocrine/paracrine signaling of the Ang/Tie2 system is important for the up-regulated angiogenesis ir the RA synovium, as well as for synoviocyte behavior, by regulating chemotactic cell movement.
61. sTie2 did not reduce goiter mass or vascular volume when used alone but was essential for complete goite inhibition.
62. sTie-2 increased significantly in the AMI patients; viability of HUVECs and tube formation area measured after stimulated with recombinant Tie-2/Fc chimera were observed to decrease, suggesting angiogenesis might be inhibited
63. expression of Ang-1 and Ang-2 is important for gastric tumor angiogenesis, and a possible autocrine/paracrine function of the angiopoietin/Tie2 system is involved in gastric cancer progression
64. present study identifies ShcA as a mediator of the anti-apoptotic activity of venous malformation -mutant Tie2
65. Tie2 was significantly overexpressed in leukemic blasts
66. Circulating levels of Ang-2 and sTie-2 receptor were detectable but invariant in women during COS cycles.

Interactions

Description .....

Product	Interactant	Other Gene	Complex	Source	Pubs
NP_000450.1	NP_001137.2	ANGPT1		HPRD	PubMe
Tie2 interacts with Ang1.					
NP_000450.1		ANGPT1		BIND	PubMe
NP_000450.1	NP_001138.1	ANGPT2		HPRD	PubMe
The receptor binding domain (RBD) of Ang2 interacts with the Tie2 ligand binding domain (LBD). This interaction was modelled on a demonstrated interaction between human Ang2 and Tie2 from an unspecified species.					
NP_000450.1	NP_001138.1	ANGPT2		BIND	PubMe
Tie2 interacts with Ang2.					
NP_000450.1	NP_001138.1	ANGPT2		BIND	PubMe

General gene information

Markers

RH68989(e-PCR)
Links: UniSTS:23344
Alternate name: L06139

SHGC-12831(e-PCR)
Links: UniSTS:78903
Alternate names: G00-677-689; GDB:677689; RH9062; TIE; UTR-03523; WI-7814; WIAF-1115

TEK_7888(e-PCR)
Links: UniSTS:466507

G10657(e-PCR)
Links: UniSTS:38250
Alternate names: CHLC.UTR_03523_L06139; CHLC.UTR_03523_L06139.P65063

TEK(e-PCR), detects polymorphism
Links: UniSTS:279460

SHGC-106556(e-PCR)
Links: UniSTS:169901

SHGC-142431(e-PCR)
Links: UniSTS:171454

TEK(e-PCR), detects polymorphism
Links: UniSTS:513742

Tek(e-PCR), detects polymorphism
Links: UniSTS:144602
Alternate name: MGI:1334605

Genotypes

See TEK SNP GeneView Report
See TEK SNP Genotype Report

Phenotypes

Venous malformations, multiple cutaneous and mucosal
MIM: 600195

Homology

Mouse, Rat
Map Viewer

GeneOntology

Provided by GOA

Function	Evidence
ATP binding	IEA
nucleotide binding	IEA
receptor activity	IEA
receptor activity PubMed 10766762	TAS
transferase activity	IEA
transmembrane receptor protein tyrosine kinase activity	IEA
transmembrane receptor protein tyrosine kinase activity PubMed 8382358	TAS

Process	Evidence
cell-cell adhesion	IEA
cell-cell signaling PubMed 8980225	TAS
cell-matrix adhesion	IEA
protein amino acid phosphorylation	IEA
regulation of angiogenesis	IEA
regulation of cell migration	IEA
regulation of cell proliferation	IEA
signal transduction PubMed 8382358	TAS
transmembrane receptor protein tyrosine kinase signaling pathway PubMed 8980225	TAS

Component	Evidence
integral to membrane	IEA

integral to plasma membrane PubMed 8382358	TAS
membrane	IEA
plasma membrane PubMed 14665640,14749497	EXP

General protein information

Preferred Names
TEK tyrosine kinase, endothelial

Names
TEK tyrosine kinase, endothelial
OTTHUMP00000021167
soluble TIE2 variant 1
soluble TIE2 variant 2

NP_000450.2
EC 2.7.10.1

NCBI Reference Sequences (RefSeq)

RefSeqs maintained independently of Annotated Genomes

These reference sequences exist independently of genome builds.

mRNA and Protein(s)

1. **NM_000459.3→NP_000450.2 TEK tyrosine kinase, endothelial precursor**

Source sequence(s)	AB208796,BC035514,DC322431,DC324016
Consensus CDS	CCDS6519.1
UniProtKB/TrEMBL	A8K6W0
UniProtKB/TrEMBL	Q8IV34

Conserved Domains (8) summary

cd00054 **Location:227–252** **Blast Score:95**	EGF_CA; Calcium-binding EGF-like domain, present in a large number of membrane-bound and extracellular (mostly animal) proteins. Many of these proteins require calcium for their biological function and calcium-binding sites have been found to be located at the...
cd00063 **Location:639–731** **Blast Score:162**	FN3; Fibronectin type 3 domain; One of three types of internal repeats found in the plasma protein fibronectin. Its tenth fibronectin type III repeat contains an RGD cell recognition sequence in a flexible loop between 2 strands. Approximately 2% of all...
cd05088 **Location:816–1118** **Blast Score:1615**	PTKc_Tie2; PTKc_Tie2: Protein Tyrosine Kinase (PTK) family; Tie2; catalytic (c) domain. The PTKc family is part of a larger superfamily that includes the catalytic domains of other kinases such as protein serine/threonine kinases, RIO kinases, and...
pfam07714 **Location:824–1092** **Blast Score:921**	Pkinase_Tyr; Protein tyrosine kinase
pfam10430 **Location:23–118** **Blast Score:456**	Ig_Tie2_1; Tie-2 Ig-like domain 1
cl00065 **Location:557–626** **Blast Score:139** **Location:444–518** **Blast Score:128**	FN3; Fibronectin type 3 domain; One of three types of internal repeats found in the plasma protein fibronectin. Its tenth fibronectin type III repeat contains an RGD cell recognition sequence in a flexible loop between 2 strands. Approximately 2% of all...
cl00093 **Location:370–442** **Blast Score:98**	IG; Immunoglobulin domain family; members are components of immunoglobulins, neuroglia, cell surface glycoproteins, such as, T-cell receptors, CD2, CD4, CD8, and membrane glycoproteins, such as, butyrophilin and chondroitin sulfate proteoglycan core...

RefSeqs of Annotated Genomes: Build 36.3

The following sections contain reference sequences that belong to a specific genome build.

Reference assembly

Genomic

1. **NC_000009.10 Reference assembly**

Range	27099286..27220172
Download	GenBank FASTA Sequence Viewer (beta)

2. **NT_008413.17**

Range	27099286..27220172
Download	GenBank FASTA Sequence Viewer (beta)

Alternate assembly (based on Celera assembly)

Genomic

1. **AC_000052.1 Alternate assembly (based on Celera assembly)**

Range	27037459..27158328
Download	GenBank FASTA Sequence Viewer (beta)

2. **NW_924062.1**

Range	26921978..27042847
Download	GenBank FASTA Sequence Viewer (beta)

Alternate assembly (based on HuRef)

Genomic

1. **AC_000141.1 Alternate assembly (based on HuRef)**

Range	27182726..27061816, complement
Download	GenBank FASTA Sequence Viewer (beta)

2. **NW_001839149.2**

Range	8806406..8685496, complement
Download	GenBank FASTA Sequence Viewer (beta)

Related Sequences

Nucleotide		Protein
Genomic	AL133411.9	CAI16055.1
Genomic	AL355432.7	None
Genomic	AL355433.6	None
Genomic	CH471071.2	EAW58571.1
		EAW58572.1
mRNA	AB086825.1	BAC45250.1
mRNA	AB208796.1	BAD92033.1
mRNA	AK291775.1	BAF84464.1
mRNA	AK294887.1	BAG57981.1
mRNA	AK295043.1	BAG58094.1
mRNA	AK308447.1	None
mRNA	AW020953.1	None
mRNA	BC035514.1	AAH35514.2
mRNA	CA392256.1	None
mRNA	DC322431.1	None
mRNA	DC324016.1	None
mRNA	EU826591.1	ACF47627.1
mRNA	EU826592.1	ACF47628.1
mRNA	H25908.1	None
mRNA	L06139.1	AAA61139.1
Synthetic	DQ892122.2	ABM83048.1
Synthetic	EU176548.1	ABW03349.1

Protein Accession	Links	
Q02763.2	GenPept	UniProtKB/Swiss-Prot
Q59HG2	GenPept	UniProtKB/TrEMBL
Q8IV34	GenPept	UniProtKB/TrEMBL
Q8IXB8	GenPept	UniProtKB/TrEMBL

Additional Links

- MIM 600221

- GeneTests for MIM: 600221
- HPRD 02571
- UCSC UCSC
- UniGene Hs.89640

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